



# Upregulation of Pro-inflammatory Cytokine Genes by Parvovirus B19 in Human Bone Marrow Mesenchymal Stem Cells

Shahin Amiri<sup>1</sup> · Amir Atashi<sup>2</sup> · Mehdi Azad<sup>3</sup> · Azin Elmi<sup>1</sup> · Mahnoosh Abbaszade Dibavar<sup>4</sup> · Monireh Ajami<sup>4</sup> · Mansoureh Ajami<sup>4</sup> · Neda Rassaei<sup>4</sup> · Razieh Mohammadihaji<sup>1</sup> · Nematollah Gheibi<sup>1</sup> 

Received: 13 January 2019 / Accepted: 4 June 2019 / Published online: 27 June 2019  
© Springer Science+Business Media, LLC, part of Springer Nature 2019

## Abstract

Chronic inflammation plays a prominent role in cancer initiation and development. On the other hand, the Inflammation can be established by a number of factors such as viral infections. Parvovirus B19 (B19V) is a pathogen with widespread infection, which infects bone marrow erythroid progenitor cells. It has been shown that B19V can also enter human bone marrow mesenchymal stem cells (BM-MSCs). In this study, we hypothesized that BM-MSCs as the main cellular component of bone marrow niche may be induced to secrete pro-inflammatory cytokines after B19V infection. BM-MSCs were cultured up to passage 3. The cells were then subjected to nucleofection to transfer a plasmid containing B19V genome. After 36 h, total RNA was extracted and the expression levels of IL-1 $\beta$ , IL-6, TNF- $\alpha$  and NF- $\kappa$ B genes were examined using qRT-PCR. Data analysis showed the significant increase in expression levels of all studied genes in the B19V-transfected cells ( $P < 0.05$ ). Although further researches are required, our findings for the first time suggest the importance of B19V infection to establish an inflammatory microenvironment in the bone marrow and its involvement in inflammation-related diseases. Finally, based on our results, molecular assay to diagnose B19V infection of BM-MSCs prior to stem cell therapy is strongly recommended.

**Keywords** Bone marrow · Chronic inflammation · Infection · Mesenchymal stem cell · Parvovirus B19

---


✉ Nematollah Gheibi  
ngheibi@qums.ac.ir

Extended author information available on the last page of the article

- Sundin M, Lindblom A, Örvell C, Barrett AJ, Sundberg B, Watz E et al (2008) Persistence of human parvovirus B19 in multipotent mesenchymal stromal cells expressing the erythrocyte P antigen: implications for transplantation. *Biol Blood Marrow Transplant* 14(10):1172–1179
- Taniguchi K, Karin M (eds) IL-6 and related cytokines as the critical lynchpins between inflammation and cancer. Elsevier, Amsterdam.
- Tewary SK, Zhao H, Deng X, Qiu J, Tang L (2014) The human parvovirus B19 non-structural protein 1 N-terminal domain specifically binds to the origin of replication in the viral DNA. *J Virol* 449:297–303
- Tolfvenstam T, Broliden K (eds) (2009) Parvovirus B19 infection. Elsevier, Amsterdam
- Vasconcelos GM, Christensen BC, Houseman EA, Xiao J, Marsit CJ, Wiencke JK et al (2011) History of parvovirus B19 infection is associated with a DNA methylation signature in childhood acute lymphoblastic leukemia. *Epigenetics* 6(12):1436–1443
- Virchow R (1863) *Lymphatische Geschwülste. Die Krankhaften Geschwulste. 2: Hirschwald Berlin*, p. 563–578.
- Waldner MJ, Neurath MF (eds) (2014) Master regulator of intestinal disease: IL-6 in chronic inflammation and cancer development. Elsevier, Amsterdam
- Watanabe K, Otabe K, Shimizu N, Komori K, Mizuno M, Katano H et al (2018) High-sensitivity virus and mycoplasma screening test reveals high prevalence of parvovirus B19 infection in human synovial tissues and bone marrow. *Stem Cell Res Ther* 9(1):80
- Wong S, Young NS, Brown KE (2003) Prevalence of parvovirus B19 in liver tissue: no association with fulminant hepatitis or hepatitis-associated aplastic anemia. *J Infect Dis* 187(10):1581–1586
- Zavattoni M, Paolucci S, Sarasini A, Tassis B, Rustico M, Quarenghi A et al (2016) Diagnostic and prognostic value of molecular and serological investigation of human parvovirus B19 infection during pregnancy. *New Microbiol* 39(3):181–185
- Zhi N, Mills IP, Lu J, Wong S, Filippone C, Brown KE (2006) Molecular and functional analyses of a human parvovirus B19 infectious clone demonstrates essential roles for NS1, VP1, and the 11-kilodalton protein in virus replication and infectivity. *J Virol* 80(12):5941–5950
- Zhi N, Zádori Z, Brown KE, Tijssen P (2004) Construction and sequencing of an infectious clone of the human parvovirus B19. *Virology* 318(1):142–152

**Publisher's Note** Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.

## Affiliations

Shahin Amiri<sup>1</sup> · Amir Atashi<sup>2</sup> · Mehdi Azad<sup>3</sup> · Azin Elmi<sup>1</sup> ·  
Mahnoosh Abbaszade Dibavar<sup>4</sup> · Monireh Ajami<sup>4</sup> · Mansoureh Ajami<sup>4</sup> ·  
Neda Rassaei<sup>4</sup> · Razieh Mohammadihaji<sup>1</sup> · Nematollah Gheibi<sup>1</sup> 

<sup>1</sup> Department of Medical Biotechnology, Cellular and Molecular Research Center, Qazvin University of Medical Sciences, Qazvin 34199-15315, Iran

<sup>2</sup> Stem Cell and Tissue Engineering Research Center, Shahrood University of Medical Sciences, Shahrood, Iran

<sup>3</sup> Department of Medical Laboratory Sciences, Faculty of Allied Medicine, Qazvin University of Medical Sciences, Qazvin, Iran

<sup>4</sup> Department of Hematology and Blood Banking, Faculty of Medical Sciences, Tarbiat Modares University, Tehran, Iran